

# DIAGNOSTICS ACCELERATOR: PERIPHERAL BIOMARKERS PROGRAM

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## Advancing Peripheral Biomarkers for Alzheimer's and Related Dementias

One of the key barriers to the development of a disease-modifying treatment for Alzheimer's disease is an insufficient toolbox of biomarkers to easily and more specifically screen and diagnose patients, stage disease progression, monitor response to treatment, and improve the rigor and efficiency of clinical trials. Across diseases, clinical trials are twice as likely to succeed when patients are selected using validated biomarkers. In cancer, validated biomarkers have transformed drug development and clinical practice over the last decade. Now is the time to develop this strategy for Alzheimer's disease.

Notable advances have been made in developing biomarkers for Alzheimer's disease in recent years. Currently available imaging and CSF-based assays for beta-amyloid and tau are already used in clinical practice and clinical trials with high diagnostic accuracy. Efforts are underway in CSF to expand beyond this core set of biomarkers that correlate with disease-related proteinopathy in the brain to biomarkers that may reflect other correlates and key mediators of the disease, including inflammation, vascular injury, synaptic dysfunction, oxidative stress, among others.

However, there remains a clear and pressing need for inexpensive and minimally invasive biomarker tests to more easily and accurately screen and identify patients at the earliest stages of disease before the onset of irreversible injury and associated symptoms. Clinical biomarkers also are needed to monitor progression of the disease and assess response to treatments as they become available. Recently, ultrasensitive assays that detect beta-amyloid peptide ratios and peptide secondary structure in blood have been developed that correlate with brain and CSF amyloid load. Substantial work is still required to bring these and additional, validated, and minimally invasive biomarkers into the clinic.

Given the pathological heterogeneity of Alzheimer's disease and related dementias, this next generation of peripheral biomarkers must be able to characterize the individual's underlying pathophysiology. This will require an expansion of the biomarker panel beyond what is currently available. Developing these biomarkers will be critical for a broader characterization of pathology in patients with Alzheimer's disease by identifying different patient sub-types based on biological phenomenon.

### ADDF FUNDING PORTAL

LOG IN OR  
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### DEADLINES

*Must be received by 5:00 pm ET on the deadline date.*

#### Letter of Intent:

**September 14, 2018**

This is the final deadline for applicants to submit letters of intent. Letters of intent will be accepted and reviewed on a rolling basis up until this deadline.

#### Invited Full Proposal:

**November 16, 2018**

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## DIAGNOSTICS ACCELERATOR

Diagnostics Accelerator is a partnership of funders dedicated to accelerating the development of affordable and accessible biomarkers to diagnose Alzheimer's disease and related dementias, and to advance the development of more targeted treatments. Through translational research awards and access to consulting support from industry experts, this program will challenge the research community to develop novel biomarkers from peripheral modalities. Peripherally-

sourced biomarkers will enable greater patient tolerability, integration with existing sample testing infrastructure, and the scalability and affordability necessary for population-level screening.

Validated peripheral biomarkers will also enable more efficient clinical trials by allowing accurate identification of patients who may benefit from the therapeutic intervention under study. Once a disease-modifying therapy is approved, these diagnostics will be critical screening tools for the effective deployment of that treatment at scale. With sufficient evidence, a peripheral biomarker—or more likely a panel of markers—may achieve FDA qualification or approval as a diagnostic tool, and ultimately, even as a surrogate marker of disease in clinical research and clinical practice. Peripheral biomarkers, at a minimum, may screen for the need to do more invasive CSF testing or expensive PET imaging.

However, bringing these biomarkers to market remains a challenge. Clinical validation requires hundreds of well-characterized biosamples across multiple cohorts. These depletable resources are often difficult for researchers to acquire. Moreover, the private sector is wary to finance projects within this space. Even validated technologies like PET imaging are not reimbursed in the market due to the lack of related therapies, which is the primary basis for the creation of this venture philanthropy fund.

Notable efforts like the Foundation for the National Institutes of Health Biomarkers Consortium are already underway. The Diagnostics Accelerator will aim to complement and enhance projects currently in progress by providing additional funding for validation efforts. The crucial work that is now needed includes cross-validation, rigorous standardization of methods and assay technologies, and studies designed to test biomarkers for a specific context of use.

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## PERIPHERAL BIOMARKERS RFP

In its first request for proposals, Diagnostics Accelerator is soliciting projects to develop biomarkers for Alzheimer's disease and related dementias accessible from the periphery. Proposals addressing a range of potential clinical uses are of interest, especially tests for early screening and diagnosis, clinical trial enrichment, quantification of patient responses to therapeutics, or prediction of conversion from mild cognitive impairment to Alzheimer's disease. Applicants are encouraged to demonstrate both the technical rigor that underlies recent successes in peripheral biomarkers as well as bold and creative approaches to this longstanding challenge.

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## FUNDING PRIORITIES

**Modalities:** Blood and other peripheral markers, including saliva, urine, and ocular biomarkers are encouraged. The development of CSF and neuroimaging biomarkers will not be considered for this RFP; however, we encourage the use of these modalities to validate proposed biomarkers.

**Biomarker targets:** Proposed approaches will be evaluated on biological plausibility linking the biomarker to disease pathophysiology. Examples of target areas of interest include, *but are not limited to:*

- Neuroprotection
- Neurodegeneration
- Protein misfolding
- Synaptic integrity and/or activity
- Vascular injury and blood-brain barrier integrity
- Mitochondria and metabolic function

- Oxidative stress
- White matter changes

Other novel approaches that are supported by compelling evidence that demonstrate a rational biological connection to the disease process are encouraged.

**Context of use:** This RFP is open to all biomarker categories that will advance drug development for Alzheimer's and related dementias. These categories, as defined by the FDA, include diagnostic, monitoring, predictive, prognostic, pharmacodynamic/response, safety, and susceptibility/risk biomarkers. The expected context of use, which defines a biomarker's intended use clinically as a diagnostic or in drug development, should be described in the application. Additionally, the applicant should articulate where in the path to commercialization the study falls and what is the proposed plan forward.

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## PROJECT DETAILS

All proposals will be evaluated on scientific and technical merit, level of innovation, and investigator and organizational capabilities. Additionally, proposals will be evaluated on the following criteria:

- **Biomarker context of use** and how the biomarker will be incorporated into clinical use
- **Methodological considerations** including sample collection and storage, quality and reliability of the assay used, and strategy for maximizing reproducibility
- **Samples** should be obtained from well-characterized cohorts and when possible, should include individuals from minority and disparity populations

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Two types of projects will be supported through this RFP:

1. **Proof-of-principle** awards will support exploratory analyses of biomarkers at a small scale (e.g., 50-100 human samples) that are supported by human data demonstrating that the candidate markers correspond with disease pathophysiology. Preliminary assay validation data for the proposed studies should be included.

Generally, projects at this stage will be awarded up to \$500,000 based on stage and scope of research. However, if there is a compelling reason to go above this level, please contact us before submitting.

2. **Validation** awards will support biomarkers that need to be tested at a larger scale (e.g., 500-1000 samples) and are supported by a significant body of human data demonstrating that the biomarker(s) correspond with disease pathophysiology. Applicants should be able to address how validation studies would move the biomarker towards the clinic and should define their strategies for regulatory approval and commercial scale-up. Assays should be well developed. Proposals should consider compatibility with existing sampling infrastructure, scalability, and intellectual property position, and standard operating procedures should be in place. Validation studies should compare peripheral analytes to quantitative measurements using PET and/or CSF, going beyond comparisons to cognition alone.

Award amounts will be based on stage and scope of research.

Projects that succeed in the proof-of-principle stage may be eligible for follow-on funding in the form of a validation award.

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## ELIGIBILITY

Funding is open to researchers and clinicians worldwide at:

- **Academic medical centers and universities or nonprofits**

Industry partnerships are strongly encouraged.

- **Biotechnology companies**

Funding is provided through mission-related investments that require return on investment.

Existing companies and new spinouts are both eligible.

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## ACCESS TO CONSULTANTS

In addition to funding, the initiative will provide support from a network of consultants with industry and regulatory expertise. Consultants will be made available to both academic and biotech programs receiving funding from this award. Consultants will help awardees refine study designs and meet critical milestones. Consultants will also help to identify follow-on funding opportunities and partners that will advance biomarkers towards commercialization.

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## DATA SHARING

It is expected that data will be shared as appropriate; however, if data sharing would interfere with obtaining intellectual property protection, it can be deferred as required. Letters of support from the groups providing samples that agree to this policy should be included since many cohorts have strict data sharing requirements.

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## APPLICATION SUBMISSIONS

Review the [Application Instructions](#) for steps on applying.

### **For program-related inquiries, please contact:**

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### **For application submission inquiries, please contact:**

Grants and Mission-Related Investments Team

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Alzheimer's Drug Discovery Foundation



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